Complete Summary

GUIDELINE TITLE

Guidelines for topical photodynamic therapy: report of a workshop of the British Photodermatology Group.

BIBLIOGRAPHIC SOURCE(S)

Morton CA, Brown SB, Collins S, Ibbotson S, Jenkinson H, Kurwa H, Langmack K, McKenna K, Moseley H, Pearse AD, Stringer M, Taylor DK, Wong G, Rhodes LE. Guidelines for topical photodynamic therapy: report of a workshop of the British Photodermatology Group. Br J Dermatol 2002 Apr;146(4):552-67. [119 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Dermatological conditions that may be treated with topical photodynamic therapy including actinic keratoses, Bowens disease, basal cell carcinoma, squamous cell carcinoma, warts, acne, psoriasis, cutaneous T-cell lymphoma

GUIDELINE CATEGORY

Technology Assessment
Treatment

CLINICAL SPECIALTY

Dermatology

INTENDED USERS

Allied Health Personnel
Physicians

GUIDELINE OBJECTIVE(S)

To provide best practice recommendations for topical photodynamic therapy

TARGET POPULATION

All patients (adult and children) undergoing photodynamic therapy for dermatological conditions

INTERVENTIONS AND PRACTICES CONSIDERED

1. Topical photodynamic therapy (PDT) with 5-aminolaevulinic acid (ALA) (Other photosensitizers considered but not recommended: meso-tetraphenylporphinesulphonate tetrasodium [mTPPS] and meso-tetra[hydroxyphenyl]chlorine [mTHPC])
2. Drug protocols and delivery
3. Light sources
    - Laser
    - Light-emitting diodes (LED) array
    - Xenon arc
    - Meta halide
    - Tungsten/halogen
    - Fluorescent
4. Dosimetry

MAJOR OUTCOMES CONSIDERED

- Disease remission/resolution
- Cosmetic outcome
- Adverse effects of treatment
- Dosimetry
- Cost effectiveness

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

Ii: Evidence obtained from well-designed controlled trials without randomization

Iii: Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one centre or research group

Iiii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.

III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

IV: Evidence inadequate owing to problems of methodology

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Recommendation Grades

A. There is good evidence to support the use of the procedure.
B. There is fair evidence to support the use of the procedure.
C. There is poor evidence to support the use of the procedure.
D. There is fair evidence to support the rejection of the use of the procedure.
E. There is good evidence to support the rejection of the use of the procedure.

COST ANALYSIS

Cost Assessment of Topical Photodynamic Therapy (PDT) and Comparison With Existing Therapy

In addition to clinical efficacy, assessment of cost effectiveness is an important aspect of determining the overall benefit offered by a new therapy such as PDT. Such an assessment requires estimation of staff and equipment costs combined with number of treatments required, expectation for clearance, costs of associated morbidity, and diagnostic and follow-up requirements. Comparison of these figures with those from conventional therapy is limited by a deficiency of accurate data and difficulty placing a cost on certain outcome measures such as the relative superiority of PDT for good cosmesis. Estimated costs for treating patients with a single non-melanoma skin cancer (NMSC) lesion with 5-aminolaevulinic acid (ALA) -PDT are shown in Appendix 2 in the original guideline document.

Medical staff time would be required for an initial clinic assessment and follow-up but as these are also required for the alternative treatment options, these costs have been omitted from the current calculations. It has been observed that up to eight visits (median 4) were required to clear lesions of Bowen's disease in 68 patients presenting to one U.K. dermatology department employing a range of treatment options other than PDT. An efficiently organized ALA-PDT service offers the potential for reducing the number of visits and hence the cost of managing this disease (see Appendices 3 & 4 of original guideline document). Available estimates for cost-effectiveness indicate ALA-PDT to be generally comparable in cost with other therapies when morbidity costs in standard treatments are included, becoming more economical where multiple lesions can be treated in one irradiation field.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Draft guidelines are edited by the Therapy Guidelines and Audit Sub-committee (TGA) and subsequently returned to the task force for revision. The approved draft version is published in the quarterly British Association of Dermatologists (BAD) newsletter, and all BAD members are given the opportunity to respond, positively or negatively, but hopefully helpfully, within three months of publication. Finalised guidelines are approved by the TGA and the Executive Committee of the BAD and finally published in the British Journal of Dermatology.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The levels of evidence (I-IV) and strength of recommendation ratings (A-E) are defined at the end of the "Major Recommendations" field.

Light Sources and Dosimetry

Published studies indicate that several light sources are effective in promoting non-melanoma skin cancer applications of 5-aminolaevulinic acid-photodynamic therapy (ALA-PDT) (Strength of recommendation A, Quality of evidence IIiii). At present, no single light source is ideal for every possible indication for topical PDT. Choice should be based on the proposed clinical indications (including number and size of lesions), priorities for a portable compact source with a smaller field size vs. a bulky fixed large field-size source, flexibility, treatment times, and cost.

Indications for Topical Photodynamic Therapy

Actinic Keratoses

ALA-PDT, and possibly also methyl 5-aminolaevulinate-PDT, are effective in clearing non-hyperkeratotic actinic keratoses on the face and scalp, with response rates comparable with topical 5-fluorouracil and cryotherapy, although with a cosmetic response superior to that with cryotherapy (A, I).

Bowen's Disease

In summary, ALA-PDT is effective in Bowen's disease, achieving good cosmesis, and is at least as effective as cryotherapy or 5-fluorouracil, but with fewer adverse events. Topical PDT may offer advantages over existing modalities for large or multiple lesions, those in poor healing sites such as the lower leg, and for penile, digital, and facial lesions where existing treatments have recognized limitations (A, I).

Basal Cell Carcinoma (BCC)

Although licensing for BCC treatment is awaited, current evidence indicates topical ALA-PDT to be an effective therapy for superficial (<2 mm thick) BCC, at least as effective as cryotherapy, but with superior healing and cosmesis, and with particular advantages in large and multiple lesions (A, I).

Topical ALA-PDT is less effective for nodular BCC, and although adjunctive therapy with prior curettage or with penetration enhancers or fractionated treatment may improve results, there is no published randomized evidence of their benefit (C, IIiii).

Squamous Cell Carcinoma (SCC)

Despite a few encouraging results, in view of its metastatic potential and high recurrence rates, caution is currently advised in using topical ALA-PDT to treat SCC (D, IIiii).

Applications for Topical 5-Aminolaevulinic Acid-Photodynamic Therapy Other than in Non-Melanoma Skin Cancer

In view of limited evidence, no recommendations are proposed concerning other indications, except for breast metastases and vulval intraepithelial neoplasia (VIN), where there is currently poor evidence to support its use (C, IIiii).

A recent randomized controlled trial has demonstrated a lack of effect of ALA-PDT in alopecia areata (D, I).

Warts

Despite a report of lack of efficacy of single-treatment ALA-PDT in the treatment of viral warts, subsequent case series and comparison trials achieved clearance rates of 56-100%, and demonstrated superior efficacy of repetitive ALA-PDT compared with cryotherapy or placebo-PDT. (B, I)

Acne

The findings of a few studies provide encouraging evidence that ALA-PDT may be a useful adjunct in certain types of acne, but discomfort during treatment, crust formation, erythema, and pigmentation for up to 4 weeks after treatment may limit patient acceptance of this therapy. (B, I)

Psoriasis

At present, the optimal regimen for topical PDT for psoriasis has not been established and the limitations of variation in photosensitizer accumulation, therapeutic response, and pain preclude its use in clinical practice. (C, IIiii)

Cutaneous T-cell Lymphoma

The optimal regimen for treatment has yet to be established. (C, IIiii)

Adverse Effects

ALA-PDT has a low frequency of severe adverse effects, achieves a good cosmetic outcome, and has a low risk of carcinogenicity (B, IIiii).

Summary

Topical photodynamic therapy (PDT) is effective in the treatment of certain non-melanoma skin cancers and is under evaluation in other dermatoses. Its development has been enhanced by a low rate of adverse events and good cosmesis. 5-Aminolaevulinic acid (ALA) is the main agent used, converted within cells into the photosensitizer protoporphyrin IX, with surface illumination then triggering the photodynamic reaction. Despite the relative simplicity of the

technique, accurate dosimetry in PDT is complicated by multiple variables in drug formulation, delivery and duration of application, in addition to light-specific parameters. Several non-coherent and coherent light sources are effective in PDT. Optimal disease-specific irradiance, wavelength and total dose characteristics have yet to be established, and are compounded by difficulties comparing light sources. The carcinogenic risk of ALA-PDT appears to be low. Current evidence indicates topical PDT to be effective in actinic keratoses on the face and scalp, Bowen's disease and superficial basal cell carcinomas (BCCs). PDT may prove advantageous where size, site or number of lesions limits the efficacy and /or acceptability of conventional therapies. Topical ALA-PDT alone is a relatively poor option for both nodular BCCs and squamous cell carcinomas. Experience of the modality in other skin diseases remains limited; areas where there is potential benefit include viral warts, acne, psoriasis and cutaneous T-cell lymphoma. A recent British Photodermatology Group workshop considered published evidence on topical PDT in order to establish guidelines to promote the efficacy and safety of this increasingly practiced treatment modality.

Definitions:

Levels of Evidence

I: Evidence obtained from at least one properly designed, randomized controlled trial

IIi: Evidence obtained from well-designed controlled trials without randomization

IIii: Evidence obtained from well-designed cohort or case-control analytical studies, preferably from more than one centre or research group

IIiii: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments could also be regarded as this type of evidence.

III: Opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

IV: Evidence inadequate owing to problems of methodology

Recommendation Grades

A. There is good evidence to support the use of the procedure.
B. There is fair evidence to support the use of the procedure.
C. There is poor evidence to support the use of the procedure.
D. There is fair evidence to support the rejection of the use of the procedure.
E. There is good evidence to support the rejection of the use of the procedure.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Consistent high level quality of care for patients undergoing topical photodynamic therapy

Advantages of topical 5-aminolaevulinic acid-photodynamic therapy:

- Relatively selective treatment
- Minimal or no scarring
- Non-invasive
- Multiple lesions may be treated simultaneously
- Safe
- Out-patient procedure
- Repeated treatments possible

POTENTIAL HARMS

- Pain or discomfort, often described as burning, stinging, or prickling restricted to the illuminated area is commonly experienced during 5-aminolaevulinic acid-photodynamic therapy (ALA-PDT).
- Immediately following illumination, erythema and oedema are common, with erosion, crust formation, and healing over 2-6 weeks.
- Unlike cryotherapy or topical 5-fluorouracil, ulceration following PDT is very rare.
- A clinically obvious scar is rarely observed. Hyperpigmentation or hypopigmentation can occasionally be seen in treated areas and usually resolves within 6 months, although prolonged hyperpigmentation was observed when treating hirsutism. Permanent hair loss has been observed following ALA-PDT.
- PDT has the potential of promoting genotoxic effects, including induction of DNA strand breaks, chromosomal aberrations and alkylation of DNA, and may increase risk of skin cancer. Overall, available evidence would indicate the risk of skin cancer associated with topical PDT is low, but in view of the latent period for carcinogenesis, long-term follow-up data are required.
- Potential hazards may arise from the use of surgical lasers to deliver high-intensity light to photosensitized skin, and radiation in the blue, ultraviolet or infrared wavelengths may pose a greater potential hazard to skin and eyes.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- These guidelines have been prepared for dermatologists on behalf of the British Association of Dermatologists and reflect the best data available at the time the report was prepared. Caution should be exercised in interpreting the data; the results of future studies may require alteration of the conclusions or recommendations in this report. It may be necessary or even desirable to depart from the guidelines in the interests of specific patients and special circumstances. Just as adherence to the guidelines may not constitute defence against a claim of negligence, so deviation from them should not necessarily be deemed negligent.
- It is important that these guidelines are used appropriately in that they can only assist the practitioner and cannot be used to mandate, authorise, or outlaw treatment options. Of course it is the responsibility of the practising clinician to interpret the application of guidelines, taking into account local circumstances.
- Guidelines are inherently a fluid, dynamic process and will be updated on the British Association of Dermatologists (BAD) Web site on a regular basis.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Setting up a Topical Photodynamic Therapy (PDT) Service (preparing the business case)

1. Define the clinical need: estimation of number of suitable patients and current management approach, taking into consideration rising nonmelanoma skin cancer prevalence, complications and patient perceptions of existing therapies; local audit and pathology data helpful.
2. Describe topical PDT and its uses, its potential advantages over existing therapies, including estimated savings (e.g., reduced ulceration).
3. Include protocol and description of patient journey if new service implemented.
4. Costing PDT:
    a. Site (dedicated room vs. sharing out-patient treatment centre facilities, specific adaptations if laser source considered).
    b. Staffing: (i) medical (supervision of service, but low real-time requirement other than diagnostic and follow-up visits if performed to protocol, with clinic referral to day/phototherapy unit); (ii) nursing (hours of dermatology nurse specialist time-grade to depend on local expertise, but ability to perform entire procedure, including local anaesthesia, if required, preferable); (iii) medical records (appointments, case records-potential for similar set-up to other phototherapies).
    c. Equipment: (i) light source (purchase vs. lease, maintenance costs); (ii) photosensitizer (cost per lesion vs. drug unit cost); (iii) disposables, e.g. dressings.
5. Training: time required and arrangements proposed for training staff to become competent in PDT.
6. Proposals for prospective audit of new service.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Morton CA, Brown SB, Collins S, Ibbotson S, Jenkinson H, Kurwa H, Langmack K, McKenna K, Moseley H, Pearse AD, Stringer M, Taylor DK, Wong G, Rhodes LE. Guidelines for topical photodynamic therapy: report of a workshop of the British Photodermatology Group. Br J Dermatol 2002 Apr;146(4):552-67. [119 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2002 Apr

GUIDELINE DEVELOPER(S)

British Association of Dermatologists

SOURCE(S) OF FUNDING

British Association of Dermatologists

Funding for the workshop came from Leo Pharmaceuticals.

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the British Association of Dermatologists Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Griffiths CE. The British Association of Dermatologists guidelines for the management of skin disease Br J Dermatol. 1999 Sep;141(3):396-7.

Electronic copies: Available in Portable Document Format (PDF) from the British Association of Dermatologists Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on April 22, 2005. The information was verified by the guideline developer on August 2, 2005.

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